Amendments to the claims

1. (Currently amended) A compound of formula (I):

$$\begin{array}{c|c} R^2 & \\ N - (CH_2)_m - R^2 \\ \hline \end{array}$$

wherein

 R^1 is selected from hydrogen, C_{1-6} alkyl optionally substituted by up to three groups independently selected from C_{1-6} alkoxy, halogen and hydroxy, C_{2-6} alkenyl, C_{3-7} cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups, phenyl optionally substituted by up to three groups independently selected from R^5 and R^6 [[, and]] or heteroaryl optionally substituted by up to three groups independently selected from R^5 and R^6 .

(I)

 R^2 is selected from hydrogen, C_{1-6} alkyl [[and]] or -(CH₂) $_p$ -C₃₋₇cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups,

or $(CH_2)_m R^1$ and R^2 , together with the nitrogen atom to which they are bound, form a four- to six-membered heterocyclic ring optionally substituted by up to three $C_{1.6}$ alkyl groups;

R³ is chloro or methyl;

 R^4 is the group -NH-CO-R⁷ or -CO-NH-(CH₂)_p-R⁸;

 R^5 is selected from C_{1-6} alkyl, C_{1-6} alkoxy, -(CH₂)_p- C_{3-7} cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups, -CONR⁹ R^{10} , -NHCOR¹⁰,

 $-{\rm SO_2NHR^9}, -({\rm CH_2})_q {\rm NHSO_2R^{10}}, ~{\rm halogen}, ~{\rm CN}, ~{\rm OH}, -({\rm CH_2})_q {\rm NR^{11}R^{12}} ~{\rm [I]}, ~{\rm and} ~{\rm I]} ~{\rm Lorentz} ~{\rm trifluoromethyl};$

 $\rm R^6$ is selected from $\rm C_{1-6}$ alkyl, $\rm C_{1-6}$ alkoxy, halogen, trifluoromethyl [[and]] $\rm or$ -(CH2) o NR $^{11}\rm R^{12}$;

 R^7 is selected from hydrogen, C_{1-6} alkyl, $-(CH_2)_p$ - C_{3-7} cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups, trifluoromethyl, $-(CH_2)_r$ heteroaryl optionally substituted by R^{13} and/or R^{14} [[, and]] or $-(CH_2)_r$ henyl optionally substituted by R^{13} and/or R^{14} :

 $R^8 \ is \ selected \ from \ hydrogen, \ C_{1-6} alkyl, \ C_{3-7} cycloalkyl \ optionally$ substituted by one or more $C_{1-6} alkyl$ groups, $CONHR^9$, phenyl optionally substituted by R^{13} and/or R^{14} [], and[] or heteroaryl optionally substituted by R^{13} and/or R^{14} [].

 $\rm R^9$ and $\rm R^{10}$ are each independently selected from hydrogen [[and]] or $\rm C_{1.64}$ kyl, or

 R^9 and R^{10} , together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁵, wherein the ring is optionally substituted by up to two C_{1-6} alkyl groups;

 $R^{11} \text{ is selected from hydrogen, C}_{1-6}\text{alkyl [[and]]}\underline{\text{or}} \\ -(\text{CH}_2)_p\text{-C}_{3-7}\text{cycloalkyl optionally substituted by one or more C}_{1-6}\text{alkyl groups [[,]]}\underline{\text{i}} \\ R^{12} \text{ is selected from hydrogen [[and]]}\underline{\text{or}} \text{ C}_{1-6}\text{alkyl, or} \\ \end{cases}$

 $R^{11} \ and \ R^{12}, together with the nitrogen atom to which they are bound, form a five or six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^{15};$

 R^{13} is selected from C_{1-6} alkyl, C_{1-6} alkoxy, $-(\mathrm{CH}_2)_p\cdot C_{3-7}$ cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups, $-\mathrm{CONR}^9R^{10}$, $-\mathrm{NHCOR}^{10}$, halogen, CN, $-(\mathrm{CH}_2)_q\mathrm{NR}^{11}R^{12}$, trifluoromethyl, phenyl optionally substituted by one or more R^{14} groups [[and]] or heteroaryl optionally substituted by one or more R^{14} groups;

 $\rm R^{14}$ is selected from $\rm C_{1-6}$ alkyl, $\rm C_{1-6}$ alkoxy, halogen, trifluoromethyl [[and]] or -NR $^{11}\rm R^{12};$

 R^{15} is selected from hydrogen [[and]] or methyl;

X and Y are each independently selected from hydrogen, methyl [[and]]_or halogen;

 $\label{eq:Zisselected from -(CH_2)_8OR_{16}^{16}, -(CH_2)_8NR_{16}^{17}, -(CH_2)_8CH_2CH_2R_{16}^{16}, -(CH_2)_8COOR_{16}^{16}, -(CH_2)_8COOR_{16}^{16}, -(CH_2)_8NHCOR_{16}^{16}]], \\ -(CH_2)_8NHCONR_{16}^{16}R_{17}^{17}, -(CH_2)_8SO_2R_{16}^{16}, -(CH_2)_8SO_2NR_{16}^{16}R_{17}^{17} \text{ [[and]] or } \\ -(CH_2)_8NHSO_2R_{16}^{16};$

 R^{16} is selected from hydrogen, C_{1-6} alkyl optionally substituted by up to two hydroxy groups, $-(CH_2)_tOR^{18}$, $-(CH_2)_tNR^{18}R^{19}$, $-(CH_2)_tNHSO_2R^{18}$, $-(CH_2)_tCONR^{18}R^{19}$, $-(CH_2)_tCONR^{18}R^{1$

R17 is selected from hydrogen [[and]] or C1-6alkyl, or

 R^{16} and R^{17} , together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N- R^{15} , wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen [[and]] or $C_{1,\kappa}$ alkyl:

 $R^{18} \ and \ R^{19} \ are each independently selected from hydrogen [[and]] \underline{or}$ $C_{1-6} alkyl \ optionally \ [[substituted]] \underline{substituted} \ by up to two hydroxy groups, or$ $R^{18} \ and \ R^{19}, \ together \ with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^{15}, wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen [[and]] \underline{or}$ $C_{1-6} alkyl;$

m is selected from 0, 1, 2, 3 [[and]] or 4, wherein each carbon atom of the resulting carbon chain may be optionally substituted with up to two groups independently selected from C_{1-ca}[kyl [[and]]] or halogen:

n is 1;
p is selected from 0, 1 [[and]] or 2;
q is selected from 0, 1, 2 [[and]] or 3;
r is selected from 0 [[and]] or 1;
s is selected from 0, 1, 2, 3 and 4; and
t is selected from 1, 2, 3 [[and]] or 4;
or a pharmaceutically acceptable [[derivative]] salt thereof.

- 2. (currently amended) A compound according to claim 1 wherein R^1 is selected from C_{1-6} alkyl, C_{3-7} cycloalkyl [[and]] or phenyl optionally substituted by up to three groups selected from R^5 and R^6 .
- 3. (previously presented) A compound according to claim 1 wherein R^1 is $C_{3,6}$ cycloalkyl.
- $\mbox{4. (previously presented)} \qquad \mbox{A compound according to claim 1 wherein R^2 is hydrogen.}$
- 5. (previously presented) A compound according to claim 1 wherein m is 0 or 1.
- 6. (previously presented) A compound according to claim 1 wherein m is 1.
- (previously presented) A compound according to claim 1 wherein R⁸ is C_{3.6}cycloalkyl.
- 8. (Currently amended) A compound according to claim 1 wherein Z is selected from -(CH₂)₈OR¹⁶, -(CH₂)₈NR¹⁶R¹⁷, ||| -(CH₂)₈NHCOR¹⁶,||| -(CH₂)₈NHCOR¹⁶,||| and -(CH₂)₈NHSO₂R¹⁶.
- (Currently amended) A compound according to claim 1 substantially as hereinbefore defined with reference to any one of Examples 1 to 48;
- N^3 -cyclopropyl-5-fluoro-2'-hydroxy-6-methyl- N^4 -[(4-methylphenyl)methyl]-3,4'-biphenyldicarboxamide;
- N^3 -cyclopropyl- N^4 -(2,2-dimethylpropyl)-5-fluoro-6-methyl-2'- $\{[(methyloxy)methyl]oxy\}$ -3,4'-biphenyldicarboxamide;
- N³-cyclopropyl-5-fluoro-6-methyl-2'-{[(methyloxy)methyl]oxy}-N⁴-(2-methylpropyl)-3,4'-biphenyldicarboxamide;
- N³-cyclopropyl-N⁴-(cyclopropylmethyl)-5-fluoro-6-methyl-2'-{[(methyloxy)methyl]oxy}-3,4'-biphenyldicarboxamide;

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- N³-cyclopropyl-5-fluoro-6-methyl-2'-{[(methyloxy)methyl]oxy}-N⁴-{[4-(methyloxy)phenyl]methyl}-3,4'-biphenyldicarboxamide;
- N^3 -cyclopropyl-5-fluoro-6-methyl-2'-{[(methyloxy)methyl]oxy}- N^4 -[(1R)-1,2,2-trimethylpropyl]-3,4'-biphenyldicarboxamide;
- N³-cyclopropyl-N⁴'-[(1R)-1,2-dimethylpropyl]-5-fluoro-6-methyl-2'-{[(methyloxy)methyl]oxy}-3,4'-biphenyldicarboxamide;
- N³-cyclopropyl-N⁴-(2,2-dimethylpropyl)-5-fluoro-2'-hydroxy-6-methyl-3,4'biphenyldicarboxamide;
- N³-cyclopropyl-5-fluoro-2'-hydroxy-6-methyl-N⁴-(2-methylpropyl)-3,4'biphenyldicarboxamide;
- N³-cyclopropyl-N⁴-(cyclopropylmethyl)-5-fluoro-2'-hydroxy-6-methyl-3,4'biphenyldicarboxamide;
- N³-cyclopropyl-5-fluoro-2'-hydroxy-6-methyl-N⁴-{[4-(methyloxy)phenyl]methyl}-3,4'biphenyldicarboxamide;
- N³-cyclopropyl-5-fluoro-2'-hydroxy-6-methyl-N⁴-[(1R)-1,2,2-trimethylpropyl]-3,4'biphenyldicarboxamide;
- N³-cyclopropyl-N⁴-[(1R)-1,2-dimethylpropyl]-5-fluoro-2'-hydroxy-6-methyl-3,4'-biphenyldicarboxamide;
- N³-cyclopropyl-N⁴-(2,2-dimethylpropyl)-5-fluoro-6-methyl-2'-(methyloxy)-3,4'biphenyldicarboxamide;
- N³-cyclopropyl-5-fluoro-6-methyl-2'-(methyloxy)-N⁴-(2-methylpropyl)-3,4'biphenyldicarboxamide;
- N³-cyclopropyl-N⁴-(cyclopropylmethyl)-5-fluoro-6-methyl-2'-(methyloxy)-3,4'biphenyldicarboxamide;
- N³-cyclopropyl-5-fluoro-6-methyl-2'-(methyloxy)-N⁴--{[4-(methyloxy)phenyl]methyl}-3,4'-biphenyldicarboxamide;
- N³-cyclopropyl-5-fluoro-6-methyl-2'-(methyloxy)-N⁴-[(1R)-1,2,2-trimethylpropyl]-3,4'-biphenyldicarboxamide;
- N³-cyclopropyl-N⁴-[(1R)-1,2-dimethylpropyl]-5-fluoro-6-methyl-2'-(methyloxy)-3,4'biphenyldicarboxamide:
- N³-cyclopropyl-N⁴-(2,2-dimethylpropyl)-5-fluoro-6-methyl-2'-(propyloxy)-3,4'biphenyldicarboxamide;
- N³-cyclopropyl-2'-{[3-(dimethylamino)propyl]oxy}-N⁴-(2,2-dimethylpropyl)-5-fluoro-6-methyl-3,4'-biphenyldicarboxamide;
- N³-cyclopropyl-N⁴-(2,2-dimethylpropyl)-5-fluoro-6-methyl-2'-({2-[(methylsulfonyl)amino]ethyl}oxy)-3,4'-biphenyldicarboxamide;
- 4-[(5'-[(cyclopropylamino)carbonyl]-4-{[(2,2-dimethylpropyl)amino]carbonyl}-3'-fluoro-2'-methyl-2-biphenylyl)oxylbutanoic acid;
- $\underline{2'\text{-}[(4\text{-}amino\text{-}4\text{-}oxobutyl)oxy}]\text{-}N^3\text{-}cyclopropyl}\text{-}N^4\text{-}(2,2\text{-}dimethylpropyl)\text{-}5\text{-}fluoro\text{-}6\text{-}methyl\text{-}3,4'\text{-}biphenyldicarboxamide;}}$
- N³-cyclopropyl-N⁴·(2,2-dimethylpropyl)-5-fluoro-6-methyl-2'-{[4-(methylamino)-4-oxobutyl]oxy}-3,4'-biphenyldicarboxamide;

N³-cyclopropyl-N⁴-(2,2-dimethylpropyl)-5-fluoro-2'-[(4-hydroxybutyl)oxy]-6-methyl-3.4'-biphenyldicarboxamide;

N³-cyclopropyl-N⁴-(2,2-dimethylpropyl)-5-fluoro-6-methyl-2'-{[3-(1,3,4-oxadiazol-2-yl)propyl]oxy}-3,4'-biphenyldicarboxamide; and

N³-cyclopropyl-N⁴-(2,2-dimethylpropyl)-5-fluoro-2'-(hydroxymethyl)-6-methyl-3,4'biphenyldicarboxamide;

or a pharmaceutically acceptable [[derivative]] salt thereof.

10. (previously presented) A process for preparing a compound according to claim 1, or a pharmaceutically acceptable [[derivative]] <u>salt</u> thereof, which comprises:

(a) reacting a compound of (II)

$$O = N - (CH_2)_m - R^{\frac{1}{2}}$$

$$(Z)_n$$

(II)

in which R¹, R², Z, m and n are as defined in claim 1 and W is halogen, with a compound of formula (III)

(III)

in which R³, R⁴, X and Y are as defined in claim 1, in the presence of a catalyst, or

(b) reacting a compound of formula (VIII)

(VIII)

with a compound of formula (III) as hereinbefore defined and then reacting the acid thus formed with an amine of formula (V)

$$R^2$$
 $H \to (CH_2)_m - R^1$
(V)

in which R^1 , R^2 and m are as defined in claim 1, under amide forming conditions

(c) reacting a compound of formula (II) as hereinbefore defined with a compound of formula (IX)

(IX)

in which R³, R⁴, X and Y are as defined in claim 1, in the presence of a catalyst,

(d) reacting a compound of formula (X)

$$\bigcap_{\substack{Q \\ Q \\ X}} \bigcap_{\substack{Q \\ Q \\ Y}} \bigcap_{\substack$$

in which R³, R⁴, X, Y, Z and n are as defined in claim 1, with an amine compound of formula (V) as defined above, under amide forming conditions.

- (e) (e) final stage modification of one compound of formula (I) into another compound of formula (I), or
- (f) conversion of a compound of formula (XII)

(XII)

in which Z' is a group convertible to Z as defined in claim 1.

- 11. (currently amended) A pharmaceutical composition comprising at least one compound according to claim 1, or a pharmaceutically acceptable <u>salt [[derivative]]</u> thereof, in association with one or more pharmaceutically acceptable excipients, diluents and/or carriers.
- 12. (currently amended)

 A method for treating <u>inflammation in a human in need</u>
 thereof a condition or disease state mediated by p38 kinase activity or mediated by

eytokines produced by the activity of p38 kinase comprising administering to said human an effective amount of a patient in need thereof a compound according to claim 1. or a pharmaceutically acceptable [[derivative]] salt thereof.

13. - 14. (cancelled)

15. (currently amended) A compound of formula (IA):

(IA)

wherein

 R^1 is selected from hydrogen, $C_{1\text{--}6}$ alkyl optionally substituted by up to three groups independently selected from $C_{1\text{--}6}$ alkoxy, halogen [[and]] or hydroxy, $C_{2\text{--}6}$ alkenyl, $C_{3\text{--}7}$ cycloalkyl optionally substituted by one or more $C_{1\text{--}6}$ alkyl groups, phenyl optionally substituted by up to three groups independently selected from R^5 and R^6 , [[and]] or heteroaryl optionally substituted by up to three groups independently selected from R^5 and R^6 .

 $R^2 \ is \ selected \ from \ hydrogen, \ C_{1-6} alkyl \ [[and]] \underline{or} \ -(CH_2)_p - C_{3-7} cycloalkyl \\ optionally \ substituted \ by \ one \ or \ more \ C_{1-6} alkyl \ groups,$

or $(CH_2)_m R^1$ and R^2 , together with the nitrogen atom to which they are bound, form a four- to six-membered heterocyclic ring optionally substituted by up to three $C_{1.6}$ alkyl groups;

R³ is chloro or methyl:

R4 is the group -NH-CO-R7 or -CO-NH-(CH2)n-R8;

 R^5 is selected from C_{1-6} alkyl, C_{1-6} alkoxy, -(CH₂) $_p$ -C3_7cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups, -CONR $^9R^{10}$, -NHCOR 10 , -SO2NHR 9 , -(CH₂) $_q$ NHSO2R 10 , halogen, CN, OH, -(CH₂) $_q$ NR 11 R 12 [[, and]] or trifluoromethyl;

 $\rm R^6$ is selected from $\rm C_{1-6}$ alkyl, $\rm C_{1-6}$ alkoxy, halogen, trifluoromethyl [[and]] $\rm \underline{or}$ -(CH2) o NR 11 R 12 ;

 R^7 is selected from hydrogen, C_{1-6} alkyl, -(CH₂)_p-C₃₋₇cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups, trifluoromethyl, -(CH₂)_rheteroaryl optionally substituted by R^{13} and/or R^{14} [[, and]] or -(CH₂)_rphenyl optionally substituted by R^{13} and/or R^{14} ;

 R^8 is selected from hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups, CONHR 9 , phenyl optionally substituted by R^{13} and/or R^{14} [], and[] or heteroaryl optionally substituted by R^{13} and/or R^{14} [].

 R^9 and R^{10} are each independently selected from hydrogen [[and]] or $C_{1\text{--}}$ calkyl, or

 R^9 and R^{10} , together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^15, wherein the ring is optionally substituted by up to two C_{1-6} alkyl groups;

 $R^{11} \ is selected from \ hydrogen, \ C_{1-6} alkyl \ [land]]\underline{or} \\ -(CH_2)_p - C_{3-7} cycloalkyl \ optionally \ substituted \ by \ one \ or \ more \ C_{1-6} alkyl \ groups,$

 R^{12} is selected from hydrogen [[and]] or C_{1-6} alkyl, or

R¹¹ and R¹², together with the nitrogen atom to which they are bound, form a five or six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁵;

 R^{13} is selected from C_{1-6} alkyl, C_{1-6} alkoxy, -(CH₂)p-C₃-7cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups, -CONR $^9R^{10}$, -NHCOR 10 , halogen, CN, -(CH₂)qNR $^{11}R^{12}$, trifluoromethyl, phenyl optionally substituted by one or more R^{14} groups [[and]] or heteroaryl optionally substituted by one or more R^{14} groups:

 R^{14} is selected from $C_{1\text{--}6}$ alkyl, $C_{1\text{--}6}$ alkoxy, halogen, trifluoromethyl Handll or -NR 11 R 12 :

R¹⁵ is selected from hydrogen [[and]] or methyl;

X and Y are each independently selected from hydrogen, methyl [[and]] or halogen;

Z is selected from -(CH2)₈OR¹⁶, -(CH2)₈NR¹⁶R¹⁷, -(CH₂)₈CH₂CH₂R¹⁶, -(CH₂)₈COOR¹⁶, -(CH₂

 $-(\text{CH}_2)_8\text{NHCONR}^{16}\text{R}^{17}, -(\text{CH}_2)_8\text{SO}_2\text{R}^{16}, -(\text{CH}_2)_8\text{SO}_2\text{NR}^{16}\text{R}^{17} \text{ [[and]]}\underline{\text{or}} \\ -(\text{CH}_2)_8\text{NHSO}_2\text{R}^{16};$

 R^{16} is selected from hydrogen, C_{1-6} alkyl, $-(CH_2)_t OR^{18}$, $-(CH_2)_t NR^{18} R^{19}$, $-(CH_2)_t COOR^{18}$, $-(CH_2)_t$ heteroaryl optionally substituted by up to two groups independently selected from halogen [[and]] or C_{1-6} alkyl, [[and]] or is a $-(CH_2)_t$ phenyl optionally substituted by up to two groups independently selected from halogen, C_{1-6} alkyl [[and]] or C_{1-6} alkoxy.

R¹⁷ is selected from hydrogen [[and]] or C₁₋₆alkyl, or

 R^{16} and R^{17} , together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^{15}, wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen and $C_{1-6} alkyl;$

 R^{18} and R^{19} are each independently selected from hydrogen [[and]] or $C_{1\text{-}}\text{Galkyl},$ or

R¹⁸ and R¹⁹, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁵, wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen [[and]] or C_{1-G}alkyl;

m is selected from 0, 1, 2, 3 [[and]] or 4, wherein each carbon atom of the resulting carbon chain may be optionally substituted with up to two groups independently selected from C_{1-6} alkyl [[and]] or halogen;

n is 1;
p is selected from 0, 1 [[and]] or 2;
q is selected from 0, 1, 2 [[and]] or 3;
r is selected from 0 [[and]] or 1;
s is selected from 0, 1, 2, 3 [[and]] or 4; and
t is selected from 2, 3 [[and]] or 4;
or a pharmaceutically acceptable [[derivative]] salt thereof.

16. (new) A pharmaceutical composition comprising a compound according to claim 15, or a pharmaceutically salt thereof, in association with one or more pharmaceutically acceptable excipients, diluents and/or carriers.

17. (new) The compound according to claim 1 which is: N³-Cyclopropyl-N⁴-(2,2-dimethylpropyl)-5-fluoro-2'-(hydroxymethyl)-6-methyl-3,4'-biphenyldicarboxamide, or a pharmaceutically acceptable salt thereof.